Remarks

I. Support for Amendments and Status of the Claims

By the foregoing amendments, claims 1-4, 6-102, 104, 108, 121-132, 134-137, 139 - 174, 176-179, 185-189 and 194-219 have been cancelled without prejudice to or disclaimer of the subject matter contained therein. New claims 220-361 are sought to be entered. Support for these new claims can be found throughout the specification and claims as originally filed. Accordingly, these amendments are believed to introduce no new matter, and their entry and consideration are respectfully requested. Upon entry of these amendments, claims 220-361 are pending in the application, with claims 220 and 359 being the independent claims.

II. Summary of the Office Action

In the Office Action dated October 15, 2004, the Examiner has made or maintained one objection to, and three rejections of, the claims. Applicants respectfully offer the following remarks concerning each of these elements of the Office Action, and request reconsideration of the present application in view of these remarks.

III. Summary of the Substance of the Interview

Applicants wish to thank Examiner Mosher for the time taken to discuss this application, and the Office Action, during a personal interview held with Applicants' representatives on January 5, 2005. During this interview, the pending claims and possible claim amendments were discussed, as were the elements of the Office Action and the disclosures of the Schiller and Chackerian references. Applicants believe that the claims as currently presented overcome each of the outstanding objections and rejections.

IV. The Objection to the Claims

In the Office Action at pages 2-3, the Examiner has objected to claims 1-4, 6-11, 13-35, 43-49, 86, 100-102, 104, 108, 121-132, 134-138, 139-156, 173, 174, 176-179, 185-189, 198 and 219 as allegedly not being limited to the elected invention. Applicants respectfully traverse this objection.

According to the present Office Action, claims 1-4, 6-11, 13-35, 43-49, 86, 100-102, 104, 108, 121-132, 134-138, 139-156, 173, 174, 176-179, 185-189, 198 and 219 were examined to the extent that they read on the elected species, except for the generic linking claims. The Office Action also states that "[t]his application contains claims 12, 36-42, 50-85, 87-99, 157-172, 180-184, 194-197, and 199-218 drawn to an invention nonelected with traverse in Paper No. 9/26/2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01." Office Action at page 2, lines 11-14.

Applicants note that this objection is based on the citation of both 37 C.F.R § 1.144 and MPEP § 821.01, which relate to the situation where claims that were not elected subject to a restriction requirement under 37 C.F.R. § 1.142 are nonetheless maintained in an application. Applicants also note, however, that the claims that are objected to in this section of the Office Action were, in fact, members of the elected restriction group. In the restriction requirement of April 1, 2003, restriction was required under 37 C.F.R. § 1.142 between claims 1-189 and 194-218 of Group I, and claims 190-193 of Group II. An election of species was also required under 37 C.F.R. § 1.146. Applicants timely elected the claims of group I and species therein, with traverse, in the reply of September 26, 2003. The claims in the non-elected group were cancelled, while those to the non-elected species were maintained in the application (presumably to be withdrawn) pending allowance of the elected species and allowance of a generic linking claim, according to MPEP § 809.04.

Accordingly, Applicants respectfully assert that objected-to claims 12, 36-42, 50-85, 87-99, 157-172, 180-184, 194-197 and 199-218, were properly withdrawn from consideration as being drawn to a non-elected *species*, rather than to a non-elected *restriction group*. Applicants therefore respectfully submit that it is improper to require that these claims be *cancelled*, as they were not members of a non-elected restriction group under 37 C.F.R. § 1.142.

In any event, all of the previously pending claims have now been cancelled without prejudice or disclaimer, and substituted with a new claim set. Upon their entry, the pending claims are all drawn to compositions comprising, *inter alia*, non-natural molecular scaffolds that are based at least in part on "a virus-like particle of an RNA bacteriophage," which was the elected species within the elected restriction group. Hence, it is respectfully believed that the present claims are drawn to the invention of restriction group I that was elected with traverse in the reply filed on September 26, 2003. For at least the above reasons, the objection has been overcome; reconsideration and withdrawal are respectfully requested.

V. The Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 3, the Examiner has rejected claims 1, 100, 135 and 176 under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. By the foregoing amendments, these claims have been cancelled without prejudice or disclaimer, thus rendering moot this rejection. Nonetheless, Applicants offer the following remarks concerning this rejection as it may be applied to the new claims presented above.

The Examiner has first rejected claim 176 for reciting "6165." Applicants thank the Examiner for noting this obvious typographical error in this claim, which has not been replicated in the new claims sought to be entered. Accordingly, this portion of the rejection has been accommodated.

The Examiner has next rejected claims 1, 100 and 135 as allegedly being indefinite for reciting "virus-like particle of a bacteriophage." Applicants respectfully traverse this rejection. In any event, claims 1, 100 and 135 have been cancelled without prejudice or disclaimer, thereby rendering moot this portion of the rejection. As discussed above, the new claims sought to be entered by the foregoing amendments are all drawn to compositions comprising, *inter alia,* non-natural molecular scaffolds that are based at least in part on "a virus-like particle of an RNA bacteriophage." As noted in Applicants' previous Reply filed July 19, 2004, this phrase as used in the present claims is explicitly defined in the present specification, *e.g.*, at page 23. In addition, Applicants note that the Examiner has stated in the present Office Action that this definition in the specification is sufficient to overcome this rejection:

> Applicant argues that the phrase "virus-like particle of a bacteriophage" is defined in the specification and that the claims are therefore definite. This argument would be convincing if the claims actually referred to "a virus-like particle of an RNA-bacteriophage."

Office Action at page 3, lines 9-12. Therefore, since the claims as currently presented all recite "a virus-like particle of an RNA bacteriophage," Applicants respectfully assert that this portion of the rejection has been overcome.

In view of the foregoing remarks, Applicants respectfully assert that the claims as currently presented particularly point out and distinctly claim the subject matter regarded by Applicants as the invention. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, are respectfully requested.

VI. The Rejection Under 35 U.S.C. § 112, First Paragraph

In the Office Action at pages 3-4, the Examiner has rejected claim 176 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. By the foregoing

amendments, claim 176 has been cancelled without prejudice or disclaimer, thus rendering moot this rejection. Nonetheless, Applicants offer the following remarks concerning this rejection as it may be applied to the new claims presented above.

In making this rejection, the Examiner states that the present specification, "while being enabling for an immunogenic c[o]mposition, does not reasonably provide enablement for a vaccine as claimed." Office Action at page 3, final two lines. The Examiner also states that "[t]his rejection could be obviated by amending the claim to recite immunogenic compositions rather than vaccines." Office Action at page 4, lines 11-12. Applicants respectfully disagree with the Examiner's contentions that the present specification does not enable the full scope of "a vaccine" as originally claimed. Nonetheless, to expedite prosecution and not in acquiescence to this rejection, new claim 357 that is sought to be entered, which corresponds to cancelled claim 176, recites "an immunogenic composition" as suggested by the Examiner. Applicants respectfully contend that one of ordinary skill in the relevant arts would readily understand that such immunogenic compositions can be useful as vaccines and in any other application where it may be desirable to induce an immune response and, in particular, to produce antibodies against the antigen in the claimed compositions, by introducing the compositions of the presently claimed invention into an animal. Accordingly, Applicants do not disclaim the use of the presently claimed compositions as vaccines since, as one of ordinary skill would readily understand, a vaccine is simply one type of "immunogenic composition" that induces an immune response for a particular application.

Hence, claim 357 as currently presented does not recite "a vaccine," and instead recites "an immunogenic composition." As the Examiner has noted, this subject matter is fully enabled by the present specification. Therefore, the rejection under 35 U.S.C. § 112,

first paragraph, has been overcome; reconsideration and withdrawal are respectfully requested.

VII. The Rejection Under 35 U.S.C. § 103(a)

In the Office Action at pages 4-5, the Examiner has rejected claims 1, 100, 135 and 176 under 35 U.S.C. § 103(a) over Schiller *et al.*, US 2002/0081295 A1 (hereinafter "Schiller"). By the foregoing amendments, claims 1, 100, 135 and 176 have been cancelled, thus rendering this rejection moot. Nonetheless, Applicants offer the following remarks concerning this rejection as it may be applied to the new claims presented above.

As discussed in detail above, the present claims are drawn to compositions in which an antigen or antigenic determinant, which is a self antigen, a peptide thereof, or a fragment thereof, is attached via at least one non-peptide bond to a virus-like particle of an RNA bacteriophage to form an ordered and repetitive array. In contrast, Schiller does *not* disclose the association of antigens or antigenic determinants (or peptides or fragments thereof) via a *non-peptide bond* to a virus-like particle *of an RNA bacteriophage*. Instead, Schiller discloses two distinctly different compositions: (1) those in which an antigen is joined to the viral capsid via chemical, physical or other modification of the capsid or the antigen (termed "conjugated virus-like particles"); and (2) those in which an antigen is joined to the viral capsid via genetic engineering, such that a fusion protein is created in which the antigen is linked via a peptide bond to the virus-like particle (termed "chimeric virus-like particles" in Schiller). *See, e.g.*, Schiller at page 3, paragraph 0019.

It is also important to note that Schiller distinguishes between the virus-like particles that can be used in these two different compositions. The only virus-like particle compositions that are discussed at length and exemplified in Schiller are those that are based on bovine papillomavirus, a DNA virus. *See, e.g.*, Schiller at pages 4-8, and in the Examples

at pages 14-20. Schiller indicates that this DNA virus is useful in creating both chimeric virus-like particle compositions (*see* Schiller at pages 4-7, paragraphs 0025-0045) and conjugated virus-like particle compositions (*see* Schiller at pages 7-8, paragraphs 0046-0052). However, there is no disclosure in Schiller that RNA viruses, or virus-like particles derived from RNA viruses (such as RNA bacteriophages), can or should be similarly used in producing both conjugated and chimeric virus-like particle compositions. Instead, the only time that RNA viruses are even mentioned in Schiller is a passing reference to the use of such viruses in producing *chimeric* (but *not* conjugated) virus-like particle compositions at page 9, paragraph 0054, lines 8-18. Thus, Schiller goes to great lengths to distinguish between conjugated virus-like particle compositions and chimeric virus-like particle compositions, while demonstrating a similar distinction between the viruses that are useful in producing such compositions. Specifically, Schiller indicates that bovine papillomavirus, a DNA virus, is useful in producing both conjugated and chimeric virus-like particle compositions. However, the passing disclosure of the use of RNA viruses in Schiller is limited to preparation of *chimeric* virus-like particle compositions, in which the antigen is linked directly to the virus-like particle via a peptide bond -- Schiller does *not* disclose or suggest that RNA viruses could or should be used for the preparation of *conjugated* virus-like particle compositions in which a self antigen would be joined via chemical, physical or other modifications of the virus-like particle or the antigen, nor that RNA viruses could or should be used for the preparation of ordered and repetitive arrays in which at least one self antigen would be linked to an RNA virus-like particle via a *non-peptide bond.* One of ordinary skill reading Schiller, then, would be left with one conclusion: bovine papillomavirus, a DNA virus, is suitable for preparing arrays in which the antigen is joined to the virus-like particle via either a non-peptide bond or a peptide bond, but RNA viruses are only suitable for preparing arrays in which the antigen is produced as a fusion protein with the viral capsid,

i.e., in which the antigen is joined to the capsid protein via a peptide bond. If this were not the case, one would have expected Schiller to have disclosed the use of RNA viruses in producing *both* types of compositions, conjugated and chimeric, just as this reference did for papillomavirus-based compositions. As noted above, however, Schiller specifically fails to mention the use of RNA viruses in the preparation of compositions in which the antigen is joined to the virus-like particle via a non-peptide bond.

Hence, Schiller does not disclose the association of antigens or antigenic determinants (or peptides or fragments thereof) via a *non-peptide bond* to a virus-like particle *of an RNA bacteriophage*, as recited in the present claims. In this rejection, this deficiency in Schiller has not been remedied by reference to any other information or knowledge available to those of ordinary skill. In any event, because Schiller expressly discloses the use of papillomavirus for the production of chimeric and conjugated compositions, but only discloses the use of RNA viruses for the production of chimeric compositions, Applicants respectfully contend that Schiller actually teaches away from the presently claimed compositions, their production, and their use. That is, when one of ordinary skill reads Schiller and sees that this reference advocates using papillomavirus, a DNA virus, to prepare both types of compositions, but only advocates using RNA viruses to prepare compositions in which the antigen is linked via a peptide bond to the virus-like particle, the inescapable conclusion is that Schiller views RNA viruses as not useful for preparing compositions in which the antigen is linked via a non-peptide bond to the virus-like particle such as those that are presently claimed.

Further, Applicants note that the previously discussed Chackerian reference (*Proc. Natl. Acad. Sci. USA, 96*: 2373-2378 (1999)) also discloses only a bovine papillomavirus L1-CCR5 fusion, and does not disclose ordered and repetitive arrays of RNA bacteriophage. Furthermore, Chackerian states that one of ordinary skill in the art would *not* expect to be

able to induce antibodies against a self antigen using just any immunogenic array composition:

> It remains to be determined what specific features of these arrays are critical and how the spacing of self-antigen effects [sic] autoantibody production.

Chackerian at page 2378, col. 1, lines 1-3. Hence, Chackerian supports the conclusion that it would not have been obvious to prepare compositions in which a self antigen or antigenic determinant (or peptide or fragment thereof) is presented in the context of just *any* virus-like particle. Specifically, one of ordinary skill reading Chackerian would have concluded that the use of virus-like particles *other than* the bovine papillomavirus-based particles specifically disclosed in Schiller and/or Chackerian, such as the presently claimed compositions that are based on virus-like particles of an RNA bacteriophage, would have required additional experimentation to determine "what specific features of these arrays are critical . . . ." In this way, then, Chackerian supports the conclusion that the disclosure of conjugated bovine papillomavirus-like particles in Schiller would not have rendered obvious the presently-claimed compositions, since the findings for papillomavirus in Schiller cannot necessarily be extrapolated to arrays that are based on RNA virus-like particles.

Hence, Applicants respectfully assert that the presently claimed invention would not have been obvious over the cited references. Reconsideration and withdrawal of the rejection therefore are respectfully requested.

VIII. Other Matters

Applicants note that the Examiner has again acknowledged that the elected combination is free of the art, and that the claims would be allowable if limited to the elected species. Applicants request that the Examiner allow the claims to the elected species, including the generic linking claims, and thereafter examine and allow claims to the

nonelected species that are linked by such allowable linking claims, in accordance with MPEP § 809.04.

Finally, the Examiner has raised questions concerning Doc. No. AS95, a courtesy copy of which was enclosed with Applicants' last-filed Reply. Applicants apologize to the Examiner for any inconvenience or disclarity in referring to this document. AS95 is a document that was cited in Applicants' Fifth Supplemental Information Disclosure Statement, filed in the present matter on September 15, 2003. This reference is a copy of the International Search Report for International Appl. No. PCT/IB99/01925, issued by the European Patent Office as the International Searching Authority for that application. Applicants presume that the Examiner has considered the information listed thereon, and respectfully request that if Doc. No. AS95 still cannot be located, that the Examiner indicate such in the next Communication to Applicants, at which time a copy of the document will again be provided for the Examiner's convenience.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply, and allowance of all pending claims, are respectfully requested.

Respectfully submitted,

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